

# this week

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TAYFUN SALCI/IZUMA/ALAMY

## “Pension changes won’t end exodus”

Proposed pension changes designed to stop senior doctors leaving the NHS because of punitive taxation fall short of what’s needed, the BMA has warned. On 5 December the government published a consultation setting out changes to the NHS scheme it said would support senior staff to stay in the workforce and help the NHS tackle treatment backlogs.

The key changes include a new partial retirement option to enable doctors from age 55 to partly retire and still pay into their pension, if they reduce their pensionable pay by at least 10%; allowing retired and partly retired doctors to rejoin the scheme if they return to work or increase their hours; removing the 16 hour limit that recently retired staff can work; allowing staff working in primary care networks to access the scheme; and correcting the mismatch between two different values of inflation used in calculations so that fewer doctors are at risk of breaching the £40 000 annual allowance.

The BMA welcomed the flexibilities but said many doctors—notably those in mid-career—would still incur “sky high” tax bills from the annual or lifetime allowance.

Vishal Sharma, chair of the BMA pensions committee, said, “These proposed changes appear to be too little, too late. Although they implement some of the immediate mitigations

the BMA has been calling for, they fall well short of the long term solution the NHS desperately needs.” He cited a recent BMA survey that suggested over 40% of consultants plan to quit the NHS in the next year.

These issues were increasingly influencing the decisions of mid-career doctors, for whom partial retirement was “not an option,” Sharma said. “These doctors will still have to consider reducing the work they do to prevent incurring large punitive tax bills, and it is disingenuous of the government to suggest this will make any meaningful difference to the huge backlogs in care.”

Sharma said that although the inflation change may ease pressure this year, only a change to the Finance Act and the establishment of a tax unregistered scheme for senior NHS staff (similar to one for judges) would prevent later negative pension growth.

Will Quince, a health minister, said, “The changes we are proposing will offer senior clinicians more flexibility and control over how and when they work, putting the decision about their career in their hands. As a result, experienced senior staff will no longer feel forced to retire early.”

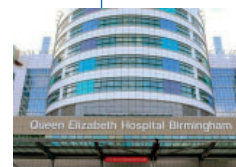
The consultation is open until 30 January.

Gareth Iacobucci, *The BMJ*  
Cite this as: *BMJ* 2022;379:o2945

**Health minister Will Quince, said the proposals will give older doctors more control over their careers**

### LATEST ONLINE

- Northern Ireland: Tackle isolation among clinicians to avoid future harms to patients, says review into neurologist
- US public health services receive \$3bn to build workforce and tackle local needs
- Calls to investigate reports of toxic culture over reporting of safety concerns at Birmingham trust



# SEVEN DAYS IN

## NHS is facing “perfect storm” as flu admissions rise 40% in a week



The number of people in hospital with flu rose by 40% in England in the week ending 27 November, with young children driving the rise, figures from NHS England show.

During the week an average of 482 patients a day were in hospital with flu, compared with 344 the previous week. This included 230 children aged under 5, which compares with 12 children at the same time last year. The highest rates of admission for flu were in children under 5 (6.88 per 100 000) and adults aged 85 or over (6.94 per 100 000).

Flu vaccine uptake in children aged 2-3 is 9% down on last year, with just under 35% having received a vaccine so far this year. Rates for pregnant women are also lower.

Overall in that week, general and acute adult bed occupancy was 95.4%, compared with 93.8% in the same week last year. And 89.6% of paediatric intensive care beds were occupied, compared with 82.5% in the same period in 2021.

Stephen Powis, NHS medical director, said, “These new figures show the NHS is facing a perfect storm, with winter virus cases rapidly increasing alongside ongoing pressures in emergency care and hugely constrained bed capacity, while hospitals continue to contend with more patients coming in than going out.”

Gareth Iacobucci, *The BMJ* Cite this as: *BMJ* 2022;379:o2920

### Workforce

#### Government is “nowhere close” to easing crisis

NHS vacancy data showed 133 446 unfilled posts in secondary care in England as of September. Latifa Patel, chair of the BMA’s representative body, said this ongoing rise in unfilled posts was a “clear sign that the government is nowhere close to getting a grip on the NHS workforce crisis.” She added, “It’s well within the government’s power to address by paying staff fairly, improving retention, and investing in proper workforce planning.”

#### Ambulance workers plan to strike before Christmas

More than 10 000 ambulance workers in England and Wales voted to strike over the government’s imposed 4% pay award, which they described as another massive real terms pay cut. The GMB union is now meeting representatives to discuss potential strike dates before Christmas. Rachel Harrison (right), GMB national secretary, said, “Ambulance workers—like other NHS workers—are on their knees. No one in the NHS takes

strike action lightly: today shows just how desperate they are. This is as much about unsafe staffing levels and patient safety as it is about pay.”

#### Transgender care Delays in England are challenged in court

Lawyers have argued in the High Court that NHS England is acting unlawfully in failing to tackle delays lasting years for transgender patients to get treatment. Mr Justice Chamberlain is expected to rule within weeks on the judicial review case brought by the Good Law Project campaigning group, along with four patients awaiting treatment and the transgender rights charity Gendered Intelligence. Their counsel, David Lock KC, claimed that NHS England was in breach of its statutory duty by failing on its target to ensure that 92% of patients started treatment within 18 weeks of referral.

#### HIV and AIDS

#### Gender inequalities “hold back” end of pandemic

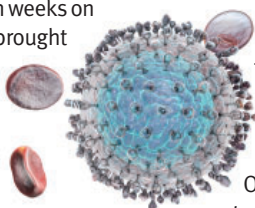
A “feminist route map” is the only effective course to ending the HIV and AIDS pandemic, said a report from the Joint United Nations Programme on

HIV and AIDS (UNAIDS), which found that gender inequalities and harmful gender norms were delaying progress. The annual report warned that the global AIDS response had been “pushed badly off track,” with new infections rising in many parts of the world, while decreases in new HIV infections and AIDS related deaths had notably slowed.

#### Hepatitis C

#### NHS is “on track” to eliminate virus by 2025

The NHS reported that it was on track to eliminate hepatitis C in 2025, five years before the World Health Organization’s 2030 target. Since a five year contract worth almost £1bn was signed to purchase antiviral drugs for thousands of patients, deaths resulting from hepatitis C—including liver disease and cancer—have fallen by 35%. John Stewart, national director for specialised commissioning at NHS England, said, “These figures demonstrate the ability of the NHS to use its commercial capabilities and purchasing power to tackle population health challenges, benefiting tens of thousands of people.”



### Digital NHS

#### Rollout of patient access to records is halted

NHS England instructed the IT system suppliers EMIS and TPP not to switch on automatic patient access to GP records at any practices that have requested more time, after talks with the BMA. The Accelerating Citizen Access to GP Data programme was supposed to see all general practices switch to automatic patient access from 1 November, but concerns over safeguarding and the extra workload led to an extension to 30 November. That deadline has been suspended until further notice.

#### HEE outlines plan for “digital first” NHS

Health Education England outlined plans to equip healthcare workers with greater digital technology skills to deliver the ambitions of the 2019 Topol review, which concluded that doctors needed training in genomics, artificial intelligence (AI), and other tech. The training will be a mix of online, digital, and face to face learning. HEE said simulation and immersive technology, AI, and haptic robotic technologies had the potential to replicate the clinical environment and interactions with patients, enabling more efficient and rapid skill development.



# MEDICINE

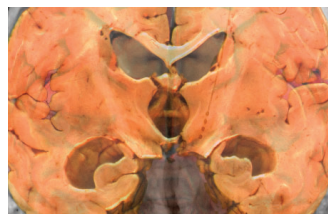
## Buildings

### BMA calls for review of UK's healthcare estate

Crumbling, outdated, and poorly laid out buildings in need of repair and modernisation are hampering doctors' efforts to provide safe and high quality care to patients, said a damning report from the BMA. More than a third of doctors (38%) who responded to a survey said that the overall physical condition of their workplace was poor or very poor, and 43% said that the condition of their workplace was having a negative effect on patient care. Latifa Patel, chair of the BMA's representative body, called the situation a "national scandal" and said that all UK governments must review the condition of the primary and secondary care estates.

## Deep brain stimulation

### Surgery is suspended at Birmingham trust



Deep brain stimulation surgery for movement disorders has been suspended indefinitely by University Hospitals Birmingham NHS Foundation Trust after an independent review of 22 procedures found poor clinical results, with most patients deriving little or no benefit. The trust commissioned the review from consultant neurosurgeons at King's College Hospital, London, after a serious incident investigation of a patient who underwent deep brain stimulation for Parkinson's disease. The external panel looked at all 22 procedures, performed on 21 patients with movement disorders from January 2017 to 1 October 2019.

Latifa Patel called the state of NHS sites a "national scandal"



## GP contract

### NICE publishes two potential QOF indicators

Two draft indicators for potential inclusion in the 2023-24 Quality and Outcomes Framework have been published by NICE. Anticoagulants for people with atrial fibrillation and an increased risk of stroke is an update to an existing indicator: it differentiates between direct acting oral anticoagulants (DOACs) and vitamin K antagonists, aiming to promote the use of DOACs over vitamin K antagonists unless DOACs are declined by the patient or are not indicated. The second is a new indicator aiming to allow more people with severe mental illness to receive recommended physical health checks.

## Assisted dying

### MPs will examine real world evidence

The Health and Social Care Committee will hold a new inquiry next year to examine different perspectives in the debate on assisted dying and assisted suicide, with a focus on the role of medical professionals, access to palliative care, safeguarding against coercion, and criteria for eligibility. MPs will also look at what can be learnt from international experiences. The committee chair, Steve Brine, said real world evidence was now available, as some form of assisted dying or assisted suicide is legal in at least 27 jurisdictions worldwide.

Cite this as: *BMJ* 2022;379:o2933

# MENTAL HEALTH

Of people who are economically inactive because of long term illness,

6 in 10 have a mental health problem. Currently 2.5 million people in the UK are inactive because of illness, the highest number on record

[IPPR]



# SIXTY SECONDS ON... CHRISTMAS WISHES



ON THE FIRST DAY OF CHRISTMAS THE NHS SENT TO ME . . .

Free staff parking at hospitals.

AND ON DAYS 2, 3, AND 4?

A proper pay rise, a quiet and comfortably furnished rest area with a kettle and microwave, hot meals at midnight . . . and free parking.

WHAT ABOUT THE NEXT THREE DAYS?

FFP3 masks for all staff, advance shift planning, holidays at the time requested . . . and free parking.

AMAZING, ARE THERE ANY MORE DAYS?

On the eighth day of Christmas the NHS put an end to GP bashing and defended its staff against the onslaught of slander in the press . . . and free parking.

I'M GETTING USED TO THIS. AND DAYS 9, 10, AND 11?

More hospital beds, a properly resourced care service, and no crumbling premises.

AND ON THE 12TH DAY?

A full complement of NHS staff—that is, all 133 446 posts in secondary care in England filled plus the promised 6000 new GPs, as well as all NHS vacancies filled in Wales, Scotland, and Northern Ireland.

WHAT IF YOU'VE BEEN NAUGHTY AND NOT NICE?

Then that will be a copy of the smash hit *Pandemic Diaries: The Inside Story of Britain's Battle Against Covid*, by former health secretary Matt Hancock (below), or a non-stop feed of the latest series of *I'm a Celebrity Get Me Out of Here*, in which Hancock finished in third place.

NOT A LUMP OF COAL, THEN?

No, but maybe some smokeless carbon neutral fuel will be seen in braziers across the UK as the NHS heads for industrial action, with nurses set to strike on 15 and 20 December. Paramedics, ambulance workers, radiographers, porters, technicians, and care workers are among other health workers who have also voted to take industrial action. And they could be followed by junior doctors, who are to vote on action in January.

Zosia Kmiotowicz, *The BMJ*

Cite this as: *BMJ* 2022;379:o2922



MARK THOMAS

## “Around 11 000 ambulances a week wait over an hour at A&E”



**Problems with urgent and emergency care are probably contributing to about a quarter of excess deaths**

Adrian Boyle

**T**he number of patients having to wait in ambulances outside English hospitals for more than an hour has risen to around 11 000 a week, the highest since records began in 2010, it has been revealed.

A BBC News analysis of NHS England data found that by late November thousands of ambulances, the equivalent to about one in seven of all arrivals, were having to wait because of hospital overcrowding.

Adrian Boyle, president of the Royal College of Emergency Medicine, said on Radio 4 *Today* on 1 December he had not seen these kinds of delays since the 1990s and he feared it was leading to excess deaths. “Last week [the ONS] recorded excess mortality across England of about 900 extra people. There are lots of causes, but we think that problems with urgent

and emergency care are probably contributing to about a quarter.”

Boyle said the problems were due to a combination of factors, adding, “The reason we’re seeing these awful long ambulance waits is because our emergency departments are full and our hospitals are full. Going back 20 years, we were able, as a country, to turn this around.

“There was the political will to establish things like the four hour access target, which was a huge piece of work and took quite a long time to get going, but it emptied the corridors and actually pushed people through the system in a way that avoided all of these problems.”

Reducing the delays relied on discharges and proper bed use, said Boyle. “At the moment there are 13 000 people waiting in hospitals, about 10% of the bed base, who are waiting to be discharged either to home with

a little bit more support or to a care facility. That’s a massive own goal. We need to reform the interface between acute hospitals and social care.”

Julie Moore, who is on the board of Worcestershire Acute Hospitals NHS Trust, told *Today* she was less convinced of the benefit of targets. “Targets can work, but they have to be applied, and you have to give people the resources to be able to deliver them, otherwise it’s pointless,” she said. “The worst part of target culture is it becomes very punitive, and then people start looking at hitting the target rather than providing the best quality of patient care that can be.”

### Varied response times

Meanwhile, the Liberal Democrat Party released details of a freedom of information request that showed wide variation in response times to life threatening calls, with patients with potential heart attack or stroke in the worst hit areas waiting an average of one hour and 40 minutes for paramedics to arrive.

A Department of Health and Social Care spokesperson said an extra £500m had been made available to speed up hospital discharge. “This will be supported by an additional £6.6bn in the NHS over the next two years to enable rapid action to improve urgent and emergency care performance towards pre-pandemic levels.”

Adrian O’Dowd, London

[Cite this as: BMJ 2022;379:o2911](#)

## Doctors slam “unjustified” attack on GP for remote working

Thousands of doctors are demanding an apology and have signed a petition condemning reports carried widely in the press on 29 November about the Cornwall based GP Justine Hall, who was working remotely for her former practice in Sussex because it was struggling to recruit a GP.

The petition, organised by the campaigning group GP Survival, said the negative press stories amounted to an “unprovoked and unjustified attack on a hardworking GP.” As *The BMJ* went to press the group was also preparing complaint letters to the

newspapers who ran the story as well as to the Independent Press Standards Organisation, which regulates them. *The BMJ* understands the press reports followed a complaint from a patient who discovered Hall was working remotely, even though other doctors at Rudgwick Medical Centre in Sussex were offering face-to-face appointments.

It has always been possible for GPs to work remotely, as there is nothing in the GMS contract to forbid it, and NHS England made telephone appointments mandatory (where possible) in the

pandemic. The petition pointed out that, by agreeing to work remotely, Hall had enabled her former practice to offer appointments.

John Hughes, chair of GP Survival and named representative on the petition, said, “Media attacks on GPs just need to stop. Dr Hall has done nothing wrong—there are hundreds and thousands of GPs working in this way.”

The petition, signed by 2504 doctors in just two days, says, “GP numbers are falling due to the increasingly difficult workload. Those who remain are left with overwhelming and unsafe

workloads, leading to more stress and burnout with even more GPs then forced to reduce hours or leave to protect their mental and physical health.

“The number of doctors dying by suicide is increasing.

“UK general practice is on the edge of destruction, and if things continue as they are, GPs will continue to leave, doctors continue to die, and patients will find it difficult to contact even a remote working GP once NHS primary care collapses.”

Adele Waters, *The BMJ*

[Cite this as: BMJ 2022;379:o2934](#)



# GPs are put on alert as strep A cases and deaths in children rise

GPs in the UK are being alerted that the group A streptococcal infection and scarlet fever season has started early and to have a high degree of clinical suspicion when assessing patients, after it was confirmed a seventh child had died.

The UK Health and Security Agency confirmed that in England so far this season five children under 10 have died within seven days of a diagnosis of an invasive strep A infection. This compares with four deaths in the 2017-18 season, the last high season for the infection. A sixth death was confirmed in Wales. The death of a seventh child, a 12 year old in London, was confirmed on 5 December.

Susan Hopkins, UKHSA's chief medical officer, told the Radio 4 *Today* programme, "The numbers we are seeing each week are not as high as we normally see at the peak of the season but are much, much higher than we have seen at this time of year for the past five years."

The UKHSA said currently there was no evidence that a new strain was circulating. The increase was most likely related to a high prevalence of circulating bacteria and social mixing.

Shiranee Sriskandan (below), professor of infectious diseases at Imperial College London, said the outbreak could potentially be linked to lack of exposure as a result of restrictions on social mixing during the pandemic. She said, "Children normally catch scarlet fever in their first year at school, if at all. We know that scarlet fever rates plummeted during 2020-21. We therefore think that school aged children may not have built up immunity to strep A, and so we now have a much larger cohort of non-immune children where strep A can circulate and cause infection. This is coupled with an unexpected rise in infections at the wrong time of the year, when winter viruses like RSV [respiratory syncytial virus] are circulating."

UKHSA guidance says, "Clinicians and health

protection teams should be mindful of potential increases in invasive disease and maintain a high degree of clinical suspicion when assessing patients, particularly those with preceding viral infection or close contacts of scarlet fever."

Group A streptococcal infections are usually mild, but a small proportion of children can develop an invasive infection where the bacteria enter the bloodstream and can cause sepsis or deep seated infections. Signs to watch for are a persistently high temperature, a pinkish or red body rash where the skin feels like sandpaper, a strawberry tongue (below), drowsiness, and not wanting to eat or drink. The recommended treatment is a 10 day course of penicillin.



A letter to GPs from UKHSA advised them "to have a low threshold to consider and empirically prescribe antibiotics to children presenting with features of GAS

infection, including where secondary to viral respiratory illness."

It also advised doctors to consider taking a throat swab to assist with differential diagnosis or if the patient is thought to be part of an outbreak. GPs should notify any cases of invasive strep A to their local health protection team so they can detect clusters and provide appropriate support.

The UKHSA said there had been a steep rise in scarlet fever notifications early in the 2022-23 season and a similar but less pronounced increase in invasive strep A infections. A total of 4622 notifications of scarlet fever were received from week 37 to 46 this season in England. In week 46 a total of 851 cases were reported. The average for the preceding five years was 186 a week.

So far England has seen 509 notifications of invasive strep A. There were 2.3 cases per 100 000 children aged 1 to 4, compared with an average of 0.5 in the pre-pandemic seasons (2017 to 2019).

Jacqui Wise, Kent

Cite this as: *BMJ* 2022;379:o2941



## Formula milk firms are exploiting legal loopholes, say campaigners

Companies are exploiting legal loopholes by selling infant milks that should be available only on prescription, campaigners have said. Babies who have conditions such as allergy or a metabolic disorder may need a specialised infant milk. These products fall under regulations that govern infant foods for special medical purposes (iFSMP), which are stricter than those for other infant formulas. However, manufacturers decide which milks are marketed as iFSMPs, with little legal oversight, says a report from the Baby Feeding Law Group (BFLG).

This means some milks, including lactose-free and anti-reflux formulas, can be bought without medical supervision. Parents may be encouraged to treat their baby with such milks rather than seek medical advice. It also means parents of babies with a true clinical need may be buying products rather than getting them on prescription.

"The baby milk industry is misusing the iFSMP category as a mechanism to make misleading health or nutrition claims which

**MANUFACTURERS DECIDE WHICH MILKS ARE MARKETING AS iFSMPs, WITH LITTLE LEGAL OVERSIGHT**

they aren't allowed to make on standard baby milks," said Robert Boyle, clinical reader in paediatric allergy at Imperial College London and a member of BFLG. "Many baby milks marketed as iFSMP have no established medical role and are used without medical supervision," he added.

The report said the use of specialised infant milks "requires ongoing medical review to ensure that they remain clinically indicated, that they are used only for as long as it is necessary and that they do not interfere with timely complementary feeding."

Two brands of lactose-free infant milk (Aptamil and SMA) and one soya based milk (SMA Soya) are marketed under infant and follow-on formula regulations, so can be sold directly to the public. But the report said they would be more appropriately marketed as iFSMPs as they have a greater potential to cause dental caries, lead to weight gain, and help to establish a preference for sweet tasting foods.

BFLG called on the government to ensure greater compliance with existing laws on marketing and to update existing legislation. The current approach was "not fit for purpose," it said.

Jacqui Wise, Kent Cite this as: *BMJ* 2022;379:o2926

# Alzheimer's: drug shows slight slowing of cognitive decline, but benefits are uncertain

**T**he monoclonal antibody lecanemab may slow cognitive decline in people with early Alzheimer's disease but is associated with higher rates of serious adverse events, trial results have shown.

Researchers from the US, UK, Canada, Japan, Singapore, Germany, and France conducted a double blind, phase 3 trial in which 898 people aged 50-90 with early Alzheimer's disease received lecanemab, while 897 received a placebo. The results, published in the *New England Journal of Medicine*, showed that lecanemab, which is administered by intravenous infusion every two weeks, reduced markers of amyloid and resulted in moderately less decline on measures of cognition and function than placebo after 18 months.

The drug's developers, Eisai and Biogen, said lecanemab works by binding to and eliminating toxic amyloid  $\beta$  aggregates thought to contribute to neurodegenerative processes in Alzheimer's disease. However, experts have said that though the findings were encouraging it is not yet known whether the drug will make a real world difference to people who have the condition.

UK Dementia Research Institute programme lead Tara Spires-Jones, said, "While this is good news from a well conducted trial, it is important to note that this is not a cure. Both groups in the trial had worsening symptoms, but people taking the drug did not decline as much in their cognitive skills." She added there was no currently accepted definition of clinically meaningful effects in the cognitive test the study used, so "it is not clear yet whether the modest reduction in decline will make a big difference to people living with dementia." Longer trials are needed to ensure benefits outweighed the risks.

## Endpoints

The trial, which was sponsored by Eisai and partly funded by Biogen, had a primary endpoint of change in score on the Clinical Dementia Rating Sum of Boxes (CDR-SB; range 0-18, with higher scores indicating greater impairment) at 18 months. At baseline the mean CDR-SB score was 3.2 in both



**It is important to note that lecanemab is not a cure** Tara Spires-Jones

groups, and all participants included in the study had evidence of amyloid on PET or by cerebrospinal fluid testing. The adjusted least squares mean change from baseline at 18 months was 1.21 with lecanemab and 1.66 with placebo (difference 0.45 (95% confidence interval 0.67 to 0.23);  $P < 0.001$ ).

Using the 14-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog14), for which a higher score indicates greater impairment, the study found that at 18 months the adjusted mean change was 4.14 in the lecanemab group and 5.58 in the placebo group (difference 1.44 (2.27 to 0.61);  $P < 0.001$ ).

A substudy involving 698 participants and using PET scans found greater reductions in brain amyloid burden with lecanemab than with placebo (difference 59.1 centiloids (62.6 to 55.6)).

Rob Howard, professor of old age psychiatry at University College London, said that while the study

**ALTHOUGH** the overall incidence of adverse events was similar in both groups, the lecanemab group had a higher incidence of serious adverse events: **14%** versus **11.3%** in the control group

## Doctors' "cry of pain" at worsening health under cuts

Doctors across the UK have told the BMA of the distress they are experiencing at witnessing people's health suffer as a result of years of "government neglect and funding cuts."

They said they were picking up the pieces of a broken social safety



net, decimated public services, poverty despite being in work, and weakened public health.

"The toll such demand takes on doctors and others could be mitigated if the government took steps to protect the nation's health," said a BMA report. It called for urgent action to protect people's economic security, properly fund public services, and tackle health inequalities.

BMA president Martin McKee said doctors' experiences amounted to a "cry of pain" and sense of helplessness for patients whose lives were worsening as

budgets for health, welfare, local government, and housing were eroded. "Doctors will not stand by while the people they treat suffer needlessly from a broken system—we are raising the alarm," he said.

## Widening inequality

The BMA said the NHS is "not prepared" for worsening levels of ill health. Its report said a decade of austerity has widened health inequalities since 2011 when long term gains in life expectancy began to stall.

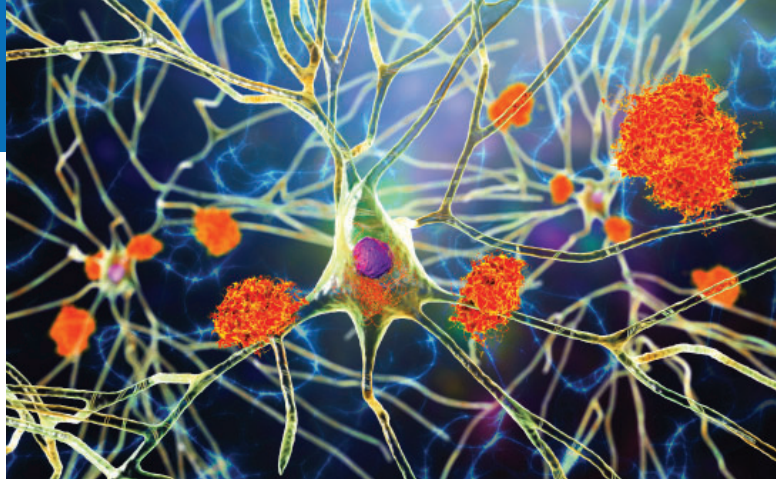
Doctors had expressed worry for disabled people and those

with cancer or other long term conditions, who face mounting difficulties covering care costs, keeping appointments, or running energy intensive equipment, and fears for people who can't afford to stop working when ill.

A general surgeon in Scotland said, "I cried after having to turn a patient away from the emergency department because there were no beds. Their condition was chronic and so not an emergency. It was winter, and they were wheelchair bound."

A Midlands psychiatrist said, "Young people are unable to





encouraged “real optimism that dementia can be beaten and one day even cured . . . the magnitude of any treatment benefits were extremely small. None of the reported results, including the primary outcome, reached accepted levels of improvement to constitute a clinically meaningful treatment effect.”

### Safety concerns

Howard also raised concerns over the study’s safety findings. He said, “The data published today indicate that six lecanemab treated patients suffered strokes during the trial, compared with two in the placebo group. Treatment therefore does carry risks . . . We need to keep looking for better and safer dementia treatments, and [these] results show that we are now on a believable path to doing so.”

Although the overall incidence of adverse events was similar in both groups, the lecanemab group had a higher incidence of serious adverse events (14% of participants versus 11.3%). The most common were infusion related reactions (1.2% v 0), amyloid related imaging abnormalities

with oedema or effusions (ARIA-E) (0.8% v 0), atrial fibrillation (0.7% v 0.3%), syncope (0.7% v 0.1%), and angina pectoris (0.7% v 0).

The most common adverse event that affected more than 10% of participants was infusion related reactions, which affected 26.4% in the lecanemab group and 7.4% in the placebo group. The lecanemab group also saw far higher rates of ARIA with cerebral microhaemorrhages, cerebral macrohaemorrhages, or superficial siderosis (17.3% v 9%), and ARIA-E (12.6% v 1.7%).

Adverse events also led more lecanemab participants to leave the trial (6.9% v 2.9%).

During the trial there were six deaths in the lecanemab group (0.7%) and seven in the placebo group (0.8%). Investigators ruled that none of the deaths were considered related to lecanemab or occurred with ARIA.

The authors said their trial results were currently limited by having only 18 months of treatment data. An open label extension study continues.

Elisabeth Mahase, *The BMJ*  
Cite this as: *BMJ* 2022;379:02912

seek support from parents stretched to make ends meet, which increases self-harm or the use of drugs to cope with life pressures. This also brings grooming into the picture, as young people become vulnerable.”

Doctors reported how they had advocated for services, facilities, and social support, only to see funds withdrawn.

The BMA said that while the uprating of benefits in line with inflation was positive, opportunities had been missed to introduce policies such as widening access to free school meals.

A Department of Health and Social Care spokesperson said, “The government has prioritised health and social care in the autumn statement, with a further £6.6bn for the NHS over the next two years.

“We have also provided more than £3.4bn this year to local authorities in England to tackle problems including alcohol use, obesity, and smoking.” They added that an extra £1200 had been given to eight million of the most vulnerable households.

Matthew Limb, London  
Cite this as: *BMJ* 2022;379:02908



**Doctors will not stand by while the people they treat suffer needlessly from a broken system**

Martin McKee

## NEWS ANALYSIS

# Why press releases do not tell the whole story

*The BMJ* stopped reporting on study results seen only in press releases in July. **Zosia Kmiotowicz** reports on its impact

It’s good to see the full data from the trial of lecanemab for Alzheimer’s disease (see left) have now been published in a peer reviewed journal. When the results were first announced by Eisai and Biogen in September it was via an “investors relations” press release. *The BMJ* did not report on these “results” because it has a new policy not to report on press releases that are not supported by information that allows proper scrutiny, such as a journal study report or a detailed research summary. Now the full paper is available it’s possible to report on the size of the effect of the findings and the data on side effects. This is important information that helps contextualise any future use of lecanemab.

Eisai has not responded to a request for a comment.

Since *The BMJ* launched its policy in July it has noted two other press releases with trial data that preceded peer reviewed publication in a journal or as a preprint.

On 1 November a Pfizer press release gave results from the Matisse study, a phase 3 international trial of its bivalent respiratory syncytial virus (RSV) vaccine candidate for maternal immunisation. Because no underlying data were supplied *The BMJ* didn’t cover the study other than to refer to it in a longer piece on MHRA’s approval of nirsevimab, a long acting monoclonal antibody, to protect newborns against RSV.

When *The BMJ* asked Pfizer why it had released data in this way, a spokesperson said, “There was a planned interim analysis and the topline data was considered material to the company. There is more data being collected and will be released via presentation or peer-reviewed paper.”

The most recent example of press release announcements occurred on 28 November when Cambridge University Hospitals Trust announced findings from the Heal-Covid trial, which is aiming to find the best treatments for people admitted to hospital with covid-19. The trial’s first finding, involving the anticoagulant apixaban, showed it made no difference to the “number of days alive and out of hospital at day 60 after randomisation,” the press release said. The trust was unable to comment before *The BMJ*’s print deadline on not providing the full data from the study.

Launching the policy, Kamran Abbasi, *The BMJ*’s editor in chief, said, “The press release has become the propagandist’s tool.” He added, “We saw it regularly at the height of the pandemic: grand announcements heralding new successful treatments and strategies, without a research paper or data analysis to support the hyperbolic claims.”

Zosia Kmiotowicz, *The BMJ* Cite this as: *BMJ* 2022;379:02938



## THE BMJ APPEAL

# Help IFRC help Earth's most vulnerable people

*The BMJ's* appeal this year is for the International Federation of Red Cross and Red Crescent Societies (IFRC). The world's largest humanitarian network brings together local Red Cross and Red Crescent societies in 192 countries and almost 15 million people volunteering for the good of humanity. They reach 160 million people every year through long term services, development programmes, and disaster response. They also work to improve global humanitarian standards and persuade leaders to act in the interests of vulnerable people.

Recent IFRC actions have included disaster relief in the earthquake hit Cianjur district in West Java, Indonesia, in November. As the power grid went out, communications such as the mobile phone network were also disrupted. Access from neighbouring Bogor district, south of Jakarta, was blocked by landslides.

In Pakistan, the August floods left almost 1000 people dead, including children, as floodwater displaced more than 3.1 million people while damaging more than half a million homes. Pakistan Red Crescent, supported by IFRC, has reached more than 584 000 people with emergency lifesaving assistance.

In Afghanistan more than 50% of schools have no latrines, handwashing facilities, or drinkable water. The Afghan Red Crescent, supported by IFRC, is working to bring safe drinking water, boys' and girls' toilets, and handwashing stations to schools across the country.

Mun-Keat Looi, international features editor, *The BMJ*

Cite this as: *BMJ* 2022;379:o2942

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1. An IFRC worker offers health checks after the earthquake in West Java, Indonesia, in November
2. A householder rescues his belongings in Pakistan after floods displaced more than 3.1 million people in August
3. Afghan Red Crescent, supported by IFRC, is working to bring safe drinking water, toilets, and handwashing stations to Afghan schools
4. Food is distributed in Biera, Mozambique, after floods this summer



GARRY LOTULLUNG / IFRC INDONESIA; PAKISTAN RCS; MEER ABDULLAH/IFRC; ANETTE SELMER-ANDRESEN/IFRC

# Domestic abuse is risk factor for suicide

Inquest in England links domestic abuse and suicide for the first time

A coroner's inquest in England has concluded the underlying cause of a 34 year old woman's suicide was domestic abuse.<sup>1</sup> She had previously attended an emergency department with cut wrists and expressed suicidal thoughts to police and other agencies, in the context of domestic abuse.

The coroner recommended greater recognition of the link between domestic abuse and suicide among first responders and improved coordination between agencies to prevent future deaths.<sup>1</sup> Although this is the first time that a coroner in the UK has cited domestic abuse as having a causal role in death by suicide, this case will be distressingly familiar to related services and researchers.<sup>2,3</sup>

The 2021 Domestic Abuse Act in England and Wales defines domestic abuse as any incident of threatening behaviour, violence, or abuse towards someone to whom the perpetrator is personally connected. This includes coercive controlling behaviour, intimate partner violence (including by a former partner), and harm perpetrated by others in the family or household. Research has largely focused on intimate partner violence, finding that it is highly gendered internationally.<sup>4</sup>

## Domestic homicides

The latest Crime Survey for England and Wales found that 74% of people subject to domestic abuse were female, and the overwhelming majority (97%) of domestic homicides were perpetrated by men.<sup>5</sup> Young women are more commonly affected than older women, including by domestic homicide and severe, repeated abuse.<sup>4</sup>

Mental health conditions, including suicidality, have a well established link with intimate partner violence.<sup>4</sup> However, more



## Domestic abuse and mental health should not be deprioritised in times of economic crisis

longitudinal data, including from low and middle income countries and marginalised groups, are required to examine context, mechanisms, and protective factors.<sup>4</sup>

But although intimate partner violence is associated with suicidal ideation, its relation with suicide is less clear because of limited data collection. Adding domestic abuse fields to healthcare records, including national electronic datasets, would drive routine identification and facilitate national studies of prevalence and the association with suicide. Intervention studies should include intimate partner violence as a potential moderator of treatment response and measure domestic abuse in new population based cohort studies.<sup>4</sup>

Many women with suicidal thoughts will have been in recent contact with health services, highlighting their role in identifying those who have been abused and providing mental health support.<sup>14</sup> The National Institute for Health and Care Excellence (NICE) recommends

that trained staff routinely ask about domestic abuse in services for women's health, addictions, mental health, and maternity care as well as in primary care when indicators of abuse, such as suicidality, emerge.<sup>15</sup> Detection of abuse and facilitation of disclosure in mental health and maternity services was already poor and has worsened since the coronavirus pandemic,<sup>16</sup> despite guidelines on whether and how to assess risk remotely.<sup>17</sup>

## Intervention, support, and prevention

Evidence suggests that training, integrated referral pathways, and system level support can increase detection, documentation, and referrals.<sup>18</sup> Health professionals and those who work in the domestic abuse sector need training to identify and respond empathetically to victims who feel suicidal and connect them to appropriate information, services, and social support.<sup>19</sup> Social support and feelings of connectedness are known to improve negative mental health symptoms associated with domestic abuse.<sup>20</sup> Co-production of services with patients and survivors is vital to ensure that trauma informed health services are accessible to and helpful for those at risk of suicide.<sup>4</sup>

Domestic abuse and mental health should not be deprioritised in times of economic crisis. Poverty adversely affects mental health, and funding for specialist third sector services and the criminal justice system has fallen since the pandemic. Interactions between poverty, abuse, and suicidal ideation mean that improving data collection, training responders, establishing referral pathways, co-producing interventions, and making healthcare services trauma informed cannot wait.

Cite this as: *BMJ* 2022;379:o2890

Find the full version with references at <http://dx.doi.org/10.1136/bmj.o2890>

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# Sri Lanka's health crisis

Urgent action is needed to maintain vital services

**S**ri Lanka is facing a severe political and economic crisis, and the health system is at risk of collapse. The crisis has been caused by years of economic mismanagement, an abrupt ban on agrochemicals in April 2021 causing a steep drop in agricultural output, and the covid-19 induced decline of the tourism industry.<sup>1</sup> In early April 2022, Sri Lanka declared itself insolvent and unable to service its overseas debt.<sup>2</sup>

Interconnected challenges, including a severe shortage of essential medicines, a worsening socioeconomic landscape, and human rights violations,<sup>3</sup> remain major threats to health in Sri Lanka.

During the first quarter of 2022, lengthy power cuts and medicines shortages undermined the provision of effective healthcare across the country.<sup>4,5</sup> Efforts to resolve these problems have fallen far short of requirements, and over 150 essential drugs remained out of stock as of November.<sup>6</sup> Additionally, essential surgical consumables and laboratory items are in short supply, affecting medical, surgical, and diagnostic capacities in all hospitals.<sup>7</sup>

## Free at the point of care

Sri Lanka's health system, traditionally free at the point of care, has been recognised as both low cost and high impact. But increasing out-of-pocket expenditure and health related inflation of nearly 40% are threatening this legacy.<sup>8</sup> Uncertain power and fuel supplies continue to compound these challenges, interrupting not only service delivery but also disease surveillance and medical supply chains.

A steep rise in poverty and unemployment in Sri Lanka has harmed population health and reduced access to care. Social determinants of health such as education, food, and income



YVES HERMAN/REUTERS/ALAMY

**Unicef estimates that over two million children in Sri Lanka require humanitarian assistance**

continue to be adversely affected, and people on the lowest incomes such as plantation sector workers have been hardest hit.<sup>9,10</sup> Public health measures to prevent the spread of infectious diseases such as covid-19 have had to contend with overcrowding on public transport because of fuel shortages.

Nearly six million Sri Lankans—three in every 10 households—are food insecure and face an 80% inflation rate for food.<sup>8,10</sup> The government has recognised food shortages as a key priority in its strategic plans.<sup>12</sup>

Unicef estimates that over two million children in Sri Lanka require humanitarian assistance.<sup>13</sup> Depression and deaths by suicide are direct consequences of the crisis,<sup>14</sup> and the mental health of children and young adults is deteriorating.<sup>1,15</sup> Prevailing human rights conditions that deny freedom of assembly and association also have a big effect on public health. Specifically, citizen protests that highlight shortages of food, medicine, and other essentials continue to face violent crackdowns by the state despite warnings from human rights organisations.<sup>3,16</sup>

Healthcare workers are personally affected by the economic and health crises facing all Sri Lankans.

Burnout is common and emigration of healthcare workers has increased. The government facilitates this migration with the short term expectation of earning foreign currency, which is likely to further weaken the health system.<sup>17</sup>

## Policy imperatives

Sri Lanka's leaders need to improve their policy on health system strengthening in both the short term and the long term. One of the most immediate concerns is a shortage of essential medicines: the current donation based stopgap solutions are not sustainable.<sup>5</sup> The government must support initiatives to increase local production of pharmaceuticals, improve national information systems to include real-time tracking of drug shortages, and establish mechanisms to stabilise power and fuel supply to essential healthcare facilities, including hospitals. It must also urgently rethink its current budgetary policy, including the budget for 2023, which continues to prioritise defence spending (\$1.1bn; £900m; €1bn) over other sectors such as health (\$880m).<sup>18</sup>

Additionally, the government must make comprehensive, sustainable plans to request and use international development assistance for health, targeted towards restoring the supply of essential medicines, supporting healthcare workers, and improving delivery of services.<sup>9</sup> Humanitarian support for the food crisis must continue, at least in the short term.<sup>19</sup>

In the longer term, Sri Lanka's current crisis is an opportunity for the government to prioritise strengthening the health system in critical areas such as primary care, to move mental health up the national agenda, and to improve social support for poor and marginalised women and children.

Cite this as: *BMJ* 2022;379:e073475

Find the full version with references at <http://dx.doi.org/10.1136/bmj-2022-073475>

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## PANDEMIC AFTERMATH

# What will happen to the orphans of covid-19?

At least 10.5 million children have been orphaned by the virus. **David Cox** reports on the global efforts to recognise and secure a future for them

**A**s soon as the covid-19 pandemic began, John Bridgeland and Gary Edson knew that it would leave a hidden toll.

The two former US government officials, who had played an instrumental role in coordinating President George W Bush's emergency plan for AIDS relief in sub-Saharan Africa, were well aware of the consequences a deadly infectious disease can wreak on children. It was the estimated 14.9 million AIDS orphans that they had in mind when co-founding Covid Collaborative, an organisation bringing together experts in health, education, and economics to shape the US response to the pandemic.

"John and Gary knew early on that there were going to be orphans with this pandemic, both globally and within the US," says Catherine Jaynes, who leads the collaborative's initiative to support covid bereaved children. "Since then, we have been working not only with the White House, but members of Congress and key partners on the ground to try to help these families and connect them to resources."

The collaborative commissioned a 2021 report, *Hidden Pain*, which provided some of the first concrete details on children orphaned by covid-19. To date, there are at least 10.5 million of these children worldwide, with studies showing that the burden has fallen heaviest on low income nations. One report in May 2022 revealed that an estimated 40.9% of covid-19 orphans are in South East Asia and 23.7% in Africa. Egypt, India, Indonesia, Nigeria, and Pakistan are the five countries bearing the brunt of the crisis.

In high income nations, it is ethnic minorities that have been hit hardest. The



*Hidden Pain* report revealed that, in the US, American Indian, Alaska Native, Native Hawaiian, and Pacific Islander children were four times more likely to have been orphaned than their white counterparts, with Black and Hispanic children two and a half times more likely. The fate of these children will represent some of the most profound long term consequences of the pandemic.

Three decades of research on AIDS orphans has shown that losing a caregiver places the bereaved children at increased risk of abuse, as well as mental health problems such as depression, anxiety, and suicide. Other long term consequences include higher rates of alcohol and other substance use disorders, worse peer relationships, and reduced employment opportunities, often as a result of dropping out of school.

But it has also provided years of learning which could be used to establish policies to help. "We literally have the research to show what works," says Susan Hillis, co-chair of the Global Reference Group on Children Affected by Covid-19 in Crisis, a non-governmental organisation linked to the World Health Organization which was established in July 2021 to develop up-to-date evidence of children affected by covid-19 associated orphanhood. "We have models that we could quickly implement if there were political will at a national, regional, and global level."

## Finding the vulnerable

One of the first challenges is identifying these vulnerable children—and very few countries have an adequate solution.

Five years ago, Brazil, with an estimated 158 600 covid-19 orphans, introduced



a box on all death certificates which indicates if a child under 18 has been left behind, making it easier for services to check on their welfare. Hillis says that this identification system has already proven invaluable for answering basic questions such as whether the child in question is safe, still in school, and has sufficient food, and could be easily adopted elsewhere.

"There are several countries interested in copying this system," she says. "For example, I'm going to Malawi and Zambia to meet with government leaders and Unicef to begin to have those discussions."

Even the US has no systematic way of tracking children who have lost a parent or caregiver. The Covid Collaborative is planning a pilot study in Utah within the next two months, which will aim to use various administrative datasets, such as birth records, to automatically detect whether there are children left behind after someone has died.

"Utah has a significant number of indigenous populations, and we know that American Indians in particular, have been hit hard by this pandemic," says Jaynes. "We're choosing a place which allows us to learn how something like this could work, but we hope to expand geographies in the next year or two."

## Securing their future

After finding orphans, there is the question of securing their future. Charles Nelson, a Harvard University neuroscientist best known for his research on institutionalised children in Romania, says that it is vital to avoid sending them to orphanages.

"We need to move with alacrity to get these children into stable, supportive





Pupils at Miracle and Victory Children Centre, a primary school for orphans from Kibera, Kenya



**Evidence shows that kin care is the absolute best option for these children**

Lucie Cluver



**We have models that we could quickly implement if there were political will**

Susan Hillis

environments,” he says. “At all costs we should avoid institutional care and aim for some kind of family care. If a relative isn’t possible, then a permanent family rather than multiple foster care placements. The bottom line is that institutional care derails development, and the longer children remain in such care, the worse the outcomes.”

In India, where there are more than two million covid-19 orphans, NGOs are now putting pressure on local governments to release data on the number of children in orphanages, as well as the number who could be legally adopted, which could make it easier for other families to take those children into their care.

Hillis is looking at models around the world in which faith communities collaborate with social services to identify children in need and help find them new homes. She cites the example of Brownsville, Texas, where African American pastors have formed a partnership with the local school and social workers to help covid-19 orphans. “They have years of history of being able to help identify relatives who might be good bets,” she says. “We’re now seeing that collaboration between local government and faith leaders replicated in 27 states.”

But simply relocating these children is not enough. Researchers say there is also an imperative to provide them with sufficient financial assistance to meet their needs. Hillis says that in three quarters of cases, orphaned children have lost their father to the virus, resulting in a substantial income deficit for the family.

“Evidence shows that kin care is the absolute best option for these children,” says Lucie Cluver, professor of child and family social work at the University of Oxford. “But

those families are now under extreme stress, and effective policies are cash transfers to help families look after children.”

## Legacy

So far, Mexico, Peru, and South Africa have all committed to providing nationwide monetary support to children orphaned by covid-19 in the form of grants or monthly stipends, while at least 11 states and some major cities across Brazil have either passed laws or are considering bills which promise to do the same. Colombia is on the way to incorporating covid-19 orphans specifically into their national child action plan priorities, creating a single national registry for these children and a comprehensive care plan which will include a periodic monetary transfer.

In some particularly impoverished nations like Zambia, however, such is the crisis wreaked first by AIDS and now covid that Hillis is calling on external organisations to step in and provide financial assistance. “Zambia has the highest prevalence of AIDS orphanhood in the world, and it now has 45 800 covid-19 orphans,” she says. “In Zambian culture, neighbouring families tend to try to take care of the children, but there are some communities where the pandemic has decimated the employment options to such an extent that nobody really has the resources to feed anyone other than their own.”

At the same time, researchers are growing frustrated that higher income countries with the resources to do more have yet to commit to specific programmes to help their own orphans. While the UK’s 15 600 covid-19 orphans will come under existing NHS social

care, there is disappointment that no specific initiatives have been announced to provide these children with targeted psychological support or counselling. “Sadly, we aren’t aware of any specific initiatives planned in the UK,” says Juliette Unwin, a researcher at Imperial College London school of public health. “We would encourage existing schemes to seek out and support these children.”

In California, the state government has allocated \$100m to create trust funds, known as baby bonds, which will provide a financial safety net for covid-19 orphans from low income backgrounds, when they reach adulthood. However, while the White House has recognised the plight of these children through a US presidential memorandum, no official support plan has been put in place at the federal level.

“We’re pushing the administration to do more,” says Jaynes. “We think that this is a topic that should resonate with President Biden—he lost his first wife and his children were left without a mother. We’re hoping that through President Biden’s State of the Union or his next budget, we can have some language that would provide for some of these opportunities.”

Hillis says it is vital that more countries start investing in more expansive schemes to help bereaved children. “We need to figure out better ways of combining the economic support with psychosocial support.”

“We’re already seeing an Ebola outbreak in Uganda, where mortality is around 50%—half of these victims will be leaving behind orphaned children,” she adds. “And this will happen again.”

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Cite this as: *BMJ* 2022;379:o2838

# AstraZeneca's covid-19 (mis)adventure and the future of vaccine equity

The pandemic brought global equality of access to the forefront of public health consciousness like never before—yet the world seems no closer to it. **Robert Fortner** asks what, if anything, has been learnt

**T**he pandemic, for a moment, wobbled the foundations of the drug industry, with calls to elevate lives above profit.

"I personally don't believe that in a time of pandemic there should be exclusive licenses," the researcher Adrian Hill declared to the *New York Times* in the spring of 2021. Hill and others at Oxford University, UK, had produced what was then the world's leading covid-19 vaccine candidate and planned to offer it to manufacturers royalty free. But the insurgency was put down before it ever got off the ground.

Oxford swiftly and exclusively licensed its technology to the UK based pharmaceutical giant AstraZeneca. The agreement did include a "non-profit" agreement: initially priced at cost, the vaccine saved more lives from covid-19 than any other in its first year of circulation. Yet the no-profit pledge also unleashed a withering crossfire—equity



**I don't believe in a time of pandemic there should be exclusive licenses**

Adrian Hill

advocates alleging grotesque hypocrisy on one side, market forces on the other.

Financial media in the US "clearly didn't like the idea of a low cost vaccine, undercutting the market," Hill told the *Financial Times*. AstraZeneca's vaccine won regulatory approval the world over, but not in the US.

Fast forward a year to 2022, and AstraZeneca seems to be exiting the stage before the pandemic ends, its good deed having earned the company a reputational thrashing. Few speak of the AstraZeneca

vaccine, while its rivals Moderna and Pfizer-BioNTech look set to profit from ongoing booster shots tailored to new covid-19 variants. These two companies have hauled in billions of dollars during the pandemic and paved the way for a new line of therapeutics based on their mRNA vaccine technology.

AstraZeneca, says Bill Enright, chief executive of the Oxford spin-out company Vaccitech, "should have been able to garner a tremendous amount of goodwill in that regard for what they were doing." He adds, "I think that will impact future initiatives."

No company seems likely to reprise AstraZeneca's corporate martyr role in future crises. And there are questions on whether Oxford's decision to partner, rather than pursue its original non-exclusive licensing plan, was a bad decision from the start. What now for the market foundations Hill sought to shake—which seem, if anything, reinforced, firmly ensconcing profit in the pandemic response?

## Big pharma middleman

Oxford's ChAd (chimpanzee adenovirus) vector technology, which saved millions of lives from covid-19, originated from years of research on malaria vaccines and had its first clinical trial in 2007. The intellectual property resided in Vaccitech, a company cofounded by Hill and a fellow Oxford researcher, Sarah Gilbert, and now led by Enright. Years ago Hill recognised that people who need malaria vaccines may lack the means to produce or pay for them, so "we need a different mechanism."

Enright says that "Vaccitech was definitely going our own way" on covid. "We actually got approval from the National Institutes of Health to get a trial started in the US," including funding, he tells *The BMJ*. Support from a European bank underwrote Vaccitech's efforts on the continent, and resources had been assigned to the UK. A Vaccitech press release from 27 March 2020 announced a clinical trial and, in parallel, an immediate vaccine manufacturing scale-up coordinated solely by Vaccitech.

But senior leaders at Oxford

## AstraZeneca—right approach, wrong partner for Oxford?

Was AstraZeneca the right partner for the Oxford Vaccine Group and its noble ideals? "The answer to that might be 'No,'" says Amanda Glassman of the Center for Global Development.

The choice was an Anglo-Swedish drug manufacturer versus picking the best partner with a background in the vaccine manufacturing and marketing business—for example, Merck. Vaccitech, the spin-out company handling Oxford's nascent technology, had been in discussions with the US based Merck in late March 2020.

Vaccitech later rued the vaccine nationalism that grew out of its tie-up with AstraZeneca the

following month. Bill Enright, Vaccitech's chief executive, when asked about what might have gone better, says, "The reality of the situation is that AstraZeneca wasn't a major vaccine player.

They had FluMist [a nasal spray influenza vaccine], but other than that they don't have a lot of vaccine expertise." As a result, AstraZeneca was "stepping into an area where they didn't have ultimate familiarity."

Glassman assumes that the choice of AstraZeneca was partly out of national security considerations—"another form of nationalism that might have resulted in less than optimal outcomes."



**Amanda Glassman believes the choice of AstraZeneca may have included national security considerations**



## Different approaches to equity

Much as the Oxford covid vaccine has roots in malaria, so do many other philanthropic endeavours—and these parallels hold lessons. Coalition for Epidemic Preparedness Innovations (CEPI) is a coalition of philanthropic partners funded by grants from Gates, the Wellcome Trust, and various governments. Nearly 20 years earlier a similar organisation was formed, anchored by the Rockefeller Foundation and geared towards one disease—the Medicines for Malaria Venture (MMV).

CEPI and MMV both steer public funding to private sector drug research in areas that for-profit companies might otherwise skip over. MMV came at a time when funders increasingly bypassed WHO, embracing public-private partnerships with the idea of getting better results for the money. Over time the private component in these partnerships has increased.

MMV, like venture capitalist investors, gets a stake in the technology developments it pays for. Companies can make and sell any malaria drug developed with MMV's support but must also license the intellectual property to MMV—patents and process knowledge. MMV is then free to pursue a scheme of manufacture and distribution tied to a goal of accessibility rather than profit.

Where MMV had Rockefeller, CEPI has Gates, which is more industry oriented—something it's been criticised for. Sarpatwari

explains, “I think there's just been a huge anger at the Gates Foundation's strong market approach to dealing with these public health issues.” If the technology difficulties had been surmountable, he says, “I really do think you would have seen some radical countries move forward”—making covid vaccines despite legal prohibitions—“but I think the risk trade-off was a little too high in this situation.”

On covid vaccines, Gates clearly sided with the drug industry in an intellectual property row: he initially dismissed calls to waive patents (“The thing that's holding things back in this case is not intellectual property,” he said in an interview with Sky News), before backtracking to concede a narrow waiver. It's arguable that if CEPI—which launched a \$2bn call to support covid vaccine candidates through clinical trials at the start of the pandemic and remains one of the most influential funders in the space—had a more MMV-type approach, such rows might have been obviated.

CEPI, for its part, says the models are based on “two completely different products (small-molecule drugs v vaccines) and disease situations (malaria v emerging infectious diseases),” a spokesperson said.

Both, however, are public-private partnerships, unlike a new player on the field: the Pandemic Antiviral Discovery

(PAD), which was announced in March to develop antiviral drugs for future pandemics, is funded by the Novo Nordisk Foundation, Open Philanthropy, and Gates. (The Novo Nordisk Foundation is the largest charitable foundation in the world, with a controlling interest in the \$230bn Danish pharmaceutical titan Novo Nordisk. Open Philanthropy originates from the fortune of the billionaire Facebook cofounder Dustin Moskovitz.)

PAD's “core” commitment to equitable access promises a “strict focus on drugs that are suitable for use in low and middle income countries.” Proposals for PAD funding can be directly submitted through the Novo Nordisk Foundation's existing system, integrating pandemic preparedness into established private sector workstreams. And unlike CEPI or MMV it has no government investments and no nation states, multilaterals, or UN agencies contributing to its purse. It's arguably freer from national interests than either of those two.

Like MMV, PAD is dealing with drugs rather than vaccines, but the challenges to developing new antivirals has parallels with the struggles in vaccine development. The PAD approach reduces nationalism, while retaining the ties with industry that are still an unavoidable necessary step in global pandemic preparedness and action.

University had already shifted in favour of partnering with a large pharmaceutical entity, as reported by the *Wall Street Journal*.

The Bill and Melinda Gates Foundation—one of the largest and most influential funders in covid vaccine development, having spent hundreds of millions of dollars—appreciated Oxford's work but not its plan for distributed manufacturing and open-source-style licensing.

“We told them a list of people to go and talk to,” said Bill Gates. Other funders, Gavi and the Coalition for Epidemic Preparedness Innovations (CEPI), also encouraged a match with a pharmaceutical partner experienced in running large clinical trials and navigating regulatory approval processes. (The Gates Foundation founded both Gavi and CEPI and continues

to fund them. AstraZeneca subsequently reached a \$750m (£652m) deal with CEPI and Gavi for its vaccine.)

Melinda Gates later told the *Washington Post* the foundation supported tiered pricing rather than open-source-style approaches. “High income countries pay a bit more than middle income, then low income,” she said. “That seems to be the right way to price a vaccine.” (In economics, tiered pricing is a form of price discriminating monopoly in which the seller can decide a price based on what buyers are able and willing to pay.)

Ameet Sarpatwari, an epidemiologist and attorney at Harvard Medical School's Center for Bioethics, believes that this framework “generally makes sense from a distributive

justice standpoint.” But he notes that, “with the billions in profits these companies are making,” pricing of the tiers “is not well calibrated.”

With the AstraZeneca partnership, Vaccitech abandoned—or at least compromised—Hill's original vision of a non-exclusive licensing plan. Enright now says that this was less a reflection of external pressure and more because the vaccine turned out to be much better than expected.

“It was [the animal study] data on the efficaciousness of the vaccine and the need to get it out to as many people as quickly as possible,” he tells *The BMJ*, the implication being that a non-exclusive licence would have been too complicated, too nascent, and perhaps not sufficiently organised to move quickly enough to save

lives at that time. Still, Enright says that Hill's original vision “was another possibility, and we were in active discussions along those lines.”

Amanda Glassman, executive vice president of the Center for Global Development, says that if Vaccitech had stuck to an open non-exclusive licence it might have been able to start ramping up capacity and sign bilateral deals with middle income countries that had their own freedom—but this is far from certain. “The Serum Institute [with which AstraZeneca signed an exclusive agreement to reproduce the vaccine for India and other countries] would not have been happy about another Indian manufacturer coming online,” Glassman says, which might have led to an exclusive arrangement in India.

## Is AstraZeneca exiting the covid-19 market?

Figures provided to *The BMJ* by the data analysis company Airfinity indicate that demand for AstraZeneca's covid vaccine decelerated abruptly near the end of 2020, resulting in cuts and halts to production—while Pfizer and Moderna have continued to sign new agreements (figs 1-3, see right).

The Serum Institute of India, an AstraZeneca manufacturing partner, recently announced it was destroying 100 million unused, expired doses, and it stopped making the vaccine in December 2021 owing to low demand.

Airfinity's analysis also shows production and deliveries of the AstraZeneca vaccine have been falling since the beginning of 2022, while it has also taken it nearly two years to fulfil orders originally agreed in 2020. In a statement to *The BMJ* AstraZeneca said that its vaccine was “currently being manufactured, though supply numbers have decreased.”

She adds that in early 2021 AstraZeneca was already experiencing manufacturing problems in supplying its first clients in Europe. This might have taken priority over supplying the non-European world. All bets were with the Serum Institute, says Glassman.

The Developing Countries Vaccine Manufacturers Network (DCVMN) is an alliance that might have jumped at non-exclusive licensing and begun producing vaccines, but Glassman isn't so sure. “The problem [by that point in 2021] was that the Oxford-AstraZeneca vaccine was not the most efficacious or sought-after vaccine,” she says, while supply issues “might also have limited how much DCVMN could have made.”

Even if Hill and colleagues had stuck to their guns over non-exclusivity, Glassman

Meanwhile, Evusheld—AstraZeneca's cocktail of monoclonal antibodies and its sole covid-19 therapy—has its own issues. The drug won approval in the US in a pre-exposure setting for immune compromised people, but it has struggled to find buyers. In the UK the Medicines and Healthcare Products Regulatory Agency approved the drug, but the government reneged on an agreement to buy it, citing “insufficient data” on the level of protection it offered against the new omicron subvariants that have come to dominate.

Regarding its covid-19 division, AstraZeneca told *The BMJ*, “We are excited about the future of this new unit.” But its pipeline for new covid vaccines and therapeutics is empty. There are no plans for variant tweaked booster jabs, leaving Pfizer and Moderna to dominate the covid vaccine market ahead of a handful of smaller, newer players such as Novavax and Valneva.

doesn't think that things would have turned out differently. “The same manufacturers that got a licence from AstraZeneca would have been interested or able to produce the vaccine under a non-exclusive deal,” she says, adding that “it would probably have taken longer, since they in theory would not have received the same support or data from AstraZeneca.”

Sarpawari believes that AstraZeneca did the right thing but wonders if the profit oriented company disincentivised itself and delivered a suboptimal performance. He asks, “Was the planning and logistics the same thing that would have gone into a blockbuster product that they would have unveiled? I don't know that.”

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Cite this as: *BMJ* 2022;379:e2592

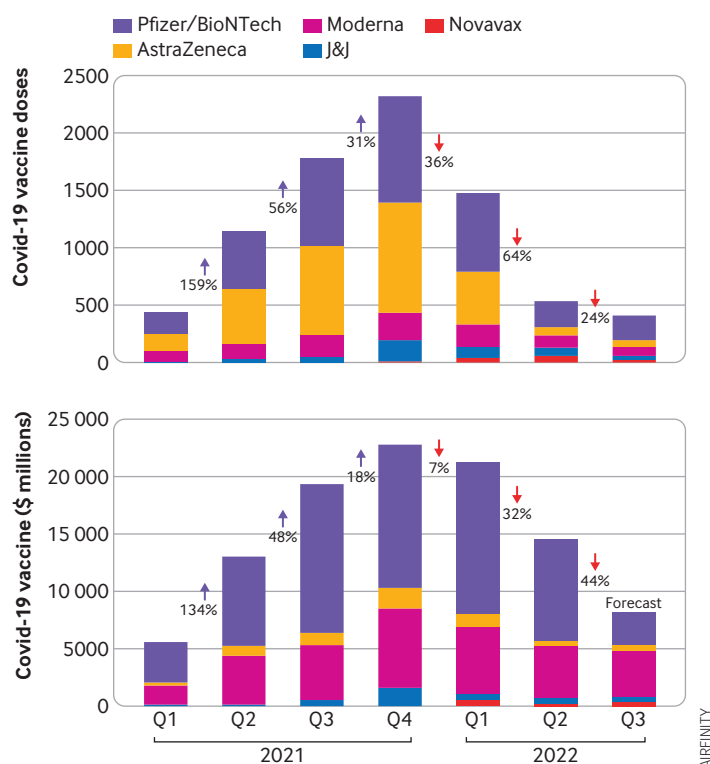


Fig 1 | Covid-19 vaccine deliveries dropped by two thirds in Q2 2022 from Q1 2022 (number of doses and revenue shown)

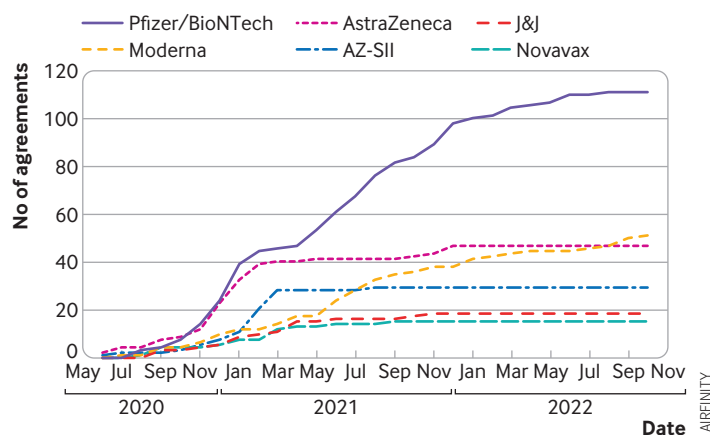


Fig 2 | The number of signed covid-19 vaccine contracts slowed down over time

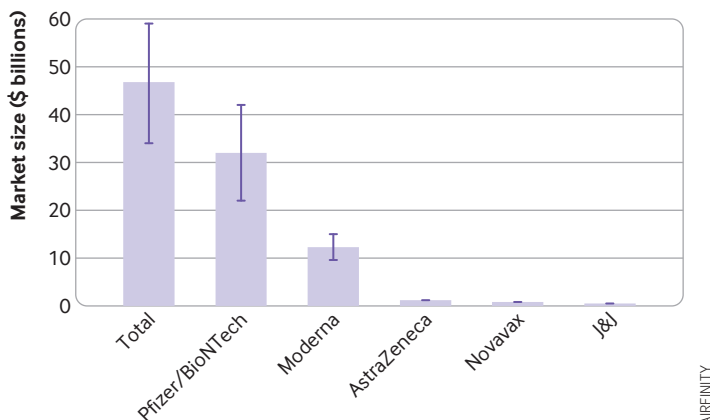


Fig 3 | Covid-19 vaccine market could reach \$47bn in 2023